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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,603	04/16/2001	Sarah S. Bacus	MBHB00-327-A	3061

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EXAMINER	
SHAHNAN SHAH, KHATOL S	

ART UNIT	PAPER NUMBER
1645	5

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,603	BACUS ET AL.	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicants' Information disclosure statement received 11/04/2002, paper # 4 is acknowledged.

2. Currently claims 1-13 are pending and under consideration.

Drawings

3. The drawings are objected to by the Draftsperson under 37 CFR 1.84 or 1.152. See attached form PTO 948.

Specification Informalities

4. The disclosure is objected to because of the following informalities:

Appropriate correction is required.

The abbreviations AKT, PTEN, are used in the specification, the full name or explanation of the above abbreviations are required when appear in the specification for the first time.

The use of the trademarks (i.e. CalBiochem, RPMI) have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claim1, 2, 6, 8, 10 and 12 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-7, 10 and 14 of copending Application No. 09/760,120. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications are drawn to a method for determining an expression level of a target protein (AKT) in a sample.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the abbreviations AKT. The full name or explanation of the above abbreviation is required when appears in the claims for the first time.

It is not clear what applicants intend in the recitation of " an optical density of staining" in claim 1.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bacus (U.S. 5,288,477) in view of Liu et al. ("Heregulin Regulation of AKT/Protein Kinase B in Breast Cancer Cells", Biochemical and Biophysical Research Communications, 1999, vol. 261, pages 897-903) and further in view of Slamon et al. (U.S. 5,846,749).

Claim 1 is drawn to a method for determining AKT protein expression amounts or activations levels in a cell or tissue sample comprising the steps of:

a) determining the amount of AKT protein in a first portion of each cell pellet prepared from at least two cell lines expressing differing amounts AKT protein,

b) staining a second portion of each said cell pellet with a detectably- labeled anti- AKT

antibody wherein the detectable label produces an optical density,

c) determining the optical density for AKT protein in the second portion of each said cell pellet,

d) producing a calibration curve of AKT protein concentration to optical density,

e) determining an optical density for AKT protein in cell or tissue sample,

f) calculating the amount of AKT protein expressed in the cell or tissue sample.

Dependent claims 2-13 embody the method of claim 1 wherein the amount of AKT protein is determined by ELISA, Northern Blot hybridization, protein microarray, immunohistochemical detection and hybridization of high density oligonucleotide arrays with cellular m RNA or cDNA prepared therefrom.

Bacus ('477) teaches a method for determining the effectiveness of a therapeutic agent in the treatment of cancer by measurement expression of cancer related proteins (human HER-2 /neu protein) comprising obtaining from a human having cancer a biopsy comprising viable malignant cells; dividing said biopsy into a first and a second portion; treating the first portion with a compound (an antibody) having specific binding affinity for said oncogene product; maintaining said first and second portions in physiologically acceptable medium for an amount of time sufficient to induce maturation in the viable malignant cells of the first portion; and

comparing the percentage of cells in the first portion which exhibit markers of terminal differentiation with the percentage of cells in the second portion, which exhibit markers of terminal differentiation (column lines 15-30 and claims 1 and 10). Bacus teaches immunohistochemical detection method (claim 6). Bacus teach two cell lines MCF-7 and AU-565 expressing different amounts of protein (column 21, lines 4-34). Bacus teaches detectably labeled antibodies (claims 6 and 11-17 and column 5). Bacus teaches that membrane bound Her-2/neu may be quantified by digitized image analysis in conjunction with fixation and staining procedures (column 11, lines 6-25). Bacus teaches that cell sample can be stained with an anti-Her-2 antibody and an additional DNA stain and that digitization of two filtered images of the single sample, one for each specific stain allows for the summation of the optical density value for the DNA stain and the optical density value for the Her-2/neu stain (column 10, lines

Bacus does not specifically teach assaying AKT protein. However, Liu et al. (Prior art of record applicants' 1449) teach detection of AKT from breast cancer cells (see pages 897-898). Liu et al. Teach AKT 1 and AKT2 (page 897), four different cell lines (page 898). Liu et al. Do not teach ELISA. However, Slamon et al. teach that a wide variety of assays can be used to detect and quantitate tissue proteins (column 4 lines 64- 67). Slamon et al. teach immunoassays including ELISA (column 5, lines 25-30), immunohistochemical staining (column 5, lines 45-

65 and column 7, lines 41-50), Northern hybridization and measuring mRNA (column 7, lines 60-67). Slamon et al. teach producing a calibration curve (column 10, lines 29-45) and calculation of determined values by comparison with the calibration curve (column 11, lies 59-67).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the method taught by Bacus, Slamon et a. and Liu et al. to determine the AKT protein expression in a cell or tissue sample by means of staining one portion of the sample with a detectably- labeled antibody with and quantitating the amount of AKT protein by comparing the optical density of the samples with a calibration curve. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of the of Bacus ('477) on the targeting measuring a breast cancer related protein marker by quantification of HER-2/neu protein by selecting optical density summation analysis in conjunction with staining procedure (see Bacus end of column 10 and beginning of column 11).

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The

examiner can normally be reached on Monday through Friday from 7:30 AM - 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

September 27, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
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10/06/03